

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.: ISPH-0215
Inventors: McKay et al.
Serial No.: 08/910,629
Filing Date: August 13, 1997
Examiner: M. Shibuya
Group Art Unit: 1635
Title: Antisense Oligonucleotide
Compositions and Methods for
Modulation of JNK Proteins

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

DECLARATION UNDER RULE 1.131

I, Robert McKay, hereby declare that:

1. I am a co-inventor of the above-identified application, filed on August 13, 1997.

2. As evidenced by the copies of my laboratory notebook pages dated October 11, 1995 attached hereto, the invention of antisense oligonucleotides targeted to JNK1 in this country was made, recorded and disclosed in confidence to another who read and understood the invention, prior to the February 14, 1997 publication date of the Seimiya et al. reference [Seimiya et al., The Journal of Biological Chemistry, 272(7):4631-4636] cited by the Examiner in an Office Action mailed on January 21, 1998 in the above-referenced application.

3. Our invention was not in public use or on sale in this country, or patented or described in a printed publication in this or any foreign country, for more than one year prior to our application. We have never abandoned our invention.

I further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

6/3/98

Date


Robert McKay

EXP #32

10/11/95

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SCREENING OF JNK 1 OLIGOS

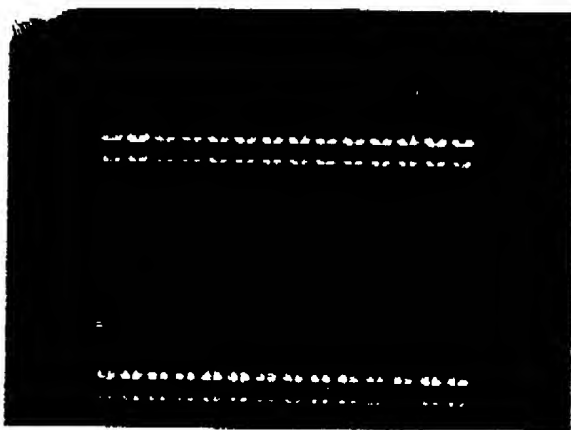
PURPOSE: IDENTIFY AN ACTIVE OLIGO TARGETING HUMAN JNK 1

PROCEDURE: HUMAN A549 CELLS WERE GROWN TO 80% CONFL. AND THEN TREATED WITH 400 nM OLIGO / 1.5 μ g/ml LPS FOR 4 HRS AND THEN WASHED AND INCUBATED FOR A FURTHER 20 HRS. RNA WAS EXTRACTED AND ANALYZED BY NORTHERN BLOTTING.

RESULTS:

| Sample # | Sample | ug/ul | ul/15 ug |
|----------|----------|-------|----------|
| 1 | No Oligo | 2 | 7.5 |
| 2 | | 2.3 | 6.5 |
| 3 | 11983 | 2.5 | 6.0 |
| 4 | | 2.7 | 5.6 |
| 5 | 12463 | 2.1 | 7.1 |
| 6 | | 1.8 | 8.3 |
| 7 | 12464 | 1.9 | 7.9 |
| 8 | | 2 | 7.5 |
| 9 | 12538 | 2.3 | 6.5 |
| 10 | | 2.5 | 6.0 |
| 11 | 12539 | 2.6 | 5.8 |
| 12 | | 1.9 | 7.9 |
| 13 | 12548 | 1.9 | 7.9 |
| 14 | | 2.6 | 5.8 |
| 15 | 12549 | 2.6 | 5.8 |
| 16 | | 2.5 | 6.0 |
| 17 | 12550 | 2.4 | 6.3 |
| 18 | | 2.1 | 7.1 |
| 19 | 12551 | 1.9 | 7.9 |
| 20 | | 1.8 | 8.3 |
| 21 | 12552 | 1.7 | 8.8 |
| 22 | | 2 | 7.5 |
| 23 | 12553 | 2.1 | 7.1 |
| 24 | | 1.9 | 7.9 |
| 25 | 12554 | 2.3 | 6.5 |
| 26 | | 2.4 | 6.3 |
| 27 | 12555 | 2.3 | 6.5 |
| 28 | | 2.1 | 7.1 |
| 29 | 12556 | 1.9 | 7.9 |
| 30 | | 1.8 | 8.3 |
| 31 | 12557 | 2.3 | 6.5 |
| 32 | | 2.5 | 6.0 |

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| #1 | #2 | #3 | #1 | #2 | #3 |
|----------|-------|----|----------|-------|-------|
| 1 NO | NO | NO | 1 NO | NO | NO |
| 2 | | | 2 | | |
| 3 12463 | 12542 | | 3 12463 | 12549 | 12554 |
| 4 | | | 4 | 12547 | 12547 |
| 5 12464 | 12543 | | 5 12464 | 12550 | 12555 |
| 6 | | | 6 | 12547 | 12463 |
| 7 12538 | 12544 | | 7 12538 | 12551 | 12556 |
| 8 | | | 8 | 12543 | 12463 |
| 9 12539 | 12545 | | 9 12539 | 12552 | 12557 |
| 10 | | | 10 | 12544 | 11982 |
| 11 12540 | 12546 | | 11 12540 | 12553 | |
| 12 | | | 12 | 12546 | 11983 |
| 13 12541 | 12547 | | 13 NO | NO | NO |
| 14 | | | 14 | | |

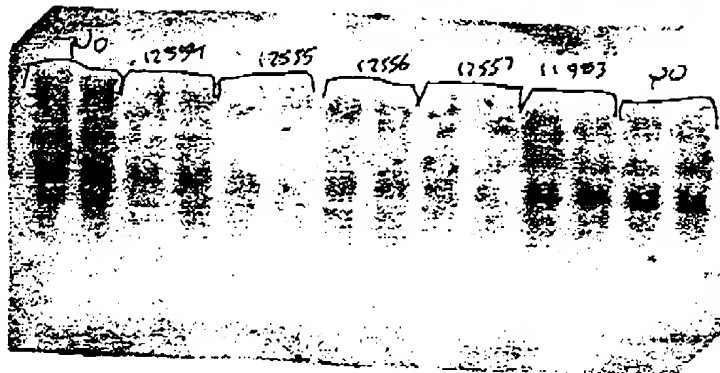
10/4/95



JNK1



JNK1



JNK1

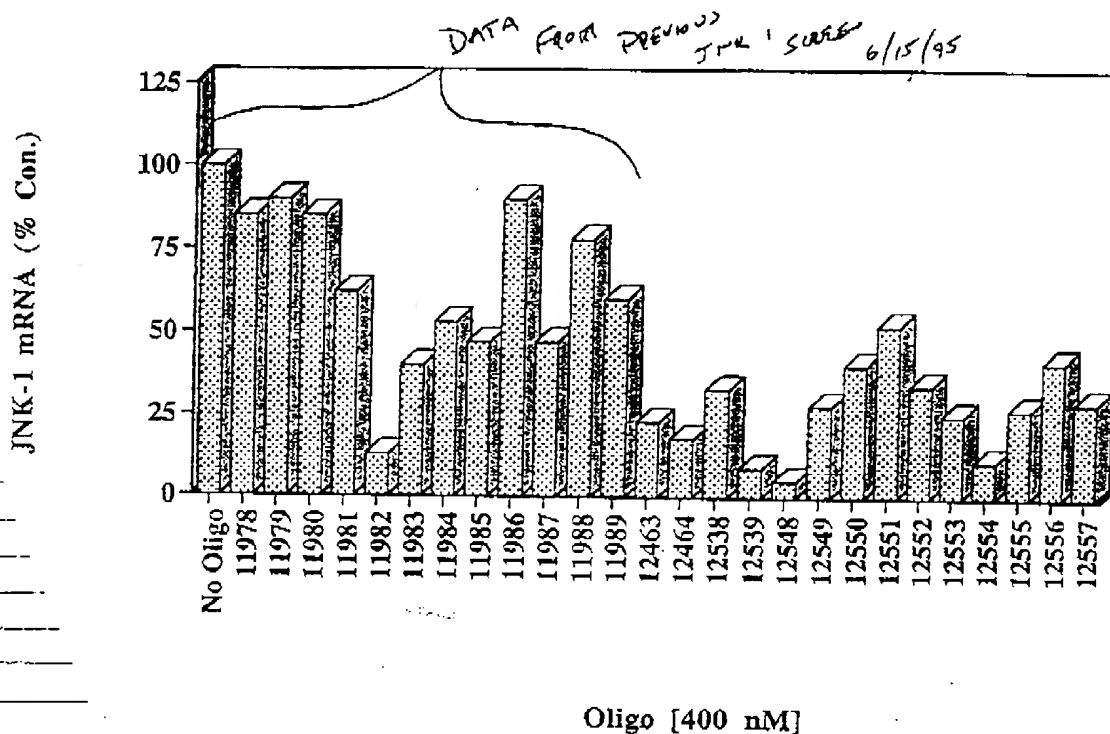
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Sheet2

| sample | ink 1 | G3PDH | Norm G3 | Norm. JNK1 | Avg | % con |
|----------|--------|------------|---------|------------|----------|-------|
| No Oligo | 115645 | 655272.941 | 0.85 | 78454 | 75698 | 100 |
| | 125543 | 647653.488 | 0.86 | 73562 | | |
| 12463 | 12546 | 1031448.15 | 0.54 | 15456 | 17410.54 | 23 |
| | 12589 | 994610.714 | 0.56 | 19854 | | |
| 12464 | 8039 | 807220.29 | 0.69 | 14265 | 13625.64 | 18 |
| | 9231 | 831316.418 | 0.67 | 12544 | | |
| 12538 | 11356 | 714079.487 | 0.78 | 26789 | 24980.34 | 33 |
| | 12354 | 742642.667 | 0.75 | 22659 | | |
| 12539 | 15654 | 944037.288 | 0.59 | 7801 | 6812.82 | 9 |
| | 17985 | 856895.385 | 0.65 | 5861 | | |
| 12548 | 13656 | 625822.472 | 0.89 | 4501 | 3784.9 | 5 |
| | 14524 | 618868.889 | 0.9 | 2953 | | |
| 12549 | 7085 | 586296.842 | 0.95 | 19215 | 21195.44 | 28 |
| | 9987 | 6120.88132 | 91 | 23541 | | |
| 12550 | 15646 | 556982 | 1 | 31564 | 30279.2 | 40 |
| | 15322 | 679246.341 | 0.82 | 29584 | | |
| 12551 | 11354 | 714079.487 | 0.78 | 36897 | 39362.96 | 52 |
| | 12451 | 598905.376 | 0.93 | 42564 | | |
| 12552 | 10963 | 568348.98 | 0.98 | 24687 | 25737.32 | 34 |
| | 11235 | 714079.487 | 0.78 | 26598 | | |
| 12553 | 18254 | 773586.111 | 0.72 | 15698 | 18924.5 | 25 |
| | 16454 | 632934.091 | 0.88 | 21548 | | |
| 12554 | 10695 | 647653.488 | 0.86 | 7821 | 8326.78 | 11 |
| | 11278 | 612068.132 | 0.91 | 8854 | | |
| 12555 | 15874 | 574208.247 | 0.97 | 22546 | 20438.46 | 27 |
| | 18658 | 625822.472 | 0.89 | 18546 | | |
| 12556 | 11256 | 640209.195 | 0.87 | 29856 | 31036.18 | 41 |
| | 14563 | 714079.487 | 0.78 | 33599 | | |
| 12557 | 9083 | 742642.667 | 0.75 | 22654 | 21952.42 | 29 |
| | 10023 | 586296.842 | 0.95 | 20154 | | |
| 11983 | 62589 | 605415.217 | 0.92 | 31222 | 30279.2 | 40 |
| | 65369 | 618868.889 | 0.9 | 29565 | | |

10/11/95

Inhibition of human JNK-1 mRNA expression in A549 cells



CONCLUSION: MULTIPLE POTENT JNK-1 OLIGOS HAVE BEEN IDENTIFIED
AND WILL BE COMPARED HEAD TO HEAD TO SELECT A
LEAD OLIGO.

[Signature] 10/11/95

| | | | |
|--|--|-----------------------------|--------------------------------|
| CERTIFICATE OF TRANSMISSION BY FACSIMILE (37 CFR 1.8) | | | Docket No. ISPH-0526 |
| Applicant(s): McKay et al. | | | |
| Serial No. 09/774,809 | Filing Date January 31, 2001 | Examiner T. Gibbs | Group Art Unit 1635 |
| Invention: ANTISENSE OLIGONUCLEOTIDE COMPOSITIONS AND METHODS FOR THE MODULATION OF JNK PROTEINS | | | |
| <p>I hereby certify that this <u>Terminal Disclaimer to Obviate a Double Patenting Rejection Over a Prior Patent</u> (Identify type of correspondence)</p> <p>is being facsimile transmitted to the United States Patent and Trademark Office (Fax. No. <u>703-872-9306</u>)</p> <p>on <u>January 3, 2003</u> (Date)</p> <p style="text-align: right;"><u>Jane Massey Licata</u> (Typed or Printed Name of Person Signing Certificate)</p> <p style="text-align: right;"><u><i>Jane Massey Licata</i></u> (Signature)</p> <p style="text-align: center;">Note: Each paper must have its own certificate of mailing.</p> | | | |

**Terminal Disclaimer To Obviate A Double
Patenting Rejection Over A Prior Patent**Docket No.
ISPH-0526

In Re Application Of: McKay et al.

Serial No.
09/774,809Filing Date
January 31, 2001Examiner
T. GibbsGroup Art Unit
1635Invention: ANTISENSE OLIGONUCLEOTIDE COMPOSITIONS AND METHODS FOR THE
MODULATION OF JNK PROTEINS

Owner of Record: Isis Pharmaceuticals, Inc.

TO THE ASSISTANT COMMISSIONER FOR PATENTS:

The above-identified owner of record of a 100 percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application, which would extend beyond the expiration date of the full statutory term defined in 35 U.S.C. 154 to 156 and 173, as presently shortened by any terminal disclaimer, of prior Patent No. 6,133,246. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the prior patent are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors and/or assigns.

In making the above disclaimer, the owner does not disclaim the terminal part of any patent granted on the instant application that would extend to the expiration date of the full statutory term as defined in 35 U.S.C. 154 to 156 and 173 of the prior patent, as presently shortened by any terminal disclaimer, in the event that it later expires for failure to pay a maintenance fee, is held unenforceable, is found invalid by a court of competent jurisdiction, is statutorily disclaimed in whole or terminally disclaimed under 37 C.F.R. 1.321, has all claims cancelled by a reexamination certificate, is reissued, or is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

Check either box 1 or 2 below, if appropriate.

1. ☐ For submissions on behalf of an organization (e.g., corporation, partnership, university, government agency, etc.), the undersigned is empowered to act on behalf of the organization.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

2. ☒ The undersigned is an attorney of record.

Dated: January 3, 2003


SignatureJane Massey Licata
Typed or Printed Name

- ☒ Terminal disclaimer fee under 37 C.F.R. 1.20(d) included.
☒ PTO suggested wording for terminal disclaimer was unchanged.
☐ Certification under 37 C.F.R. 3.73(b) is required if terminal disclaimer is signed by the assignee.

P32/REV01